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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/833,740	04/13/2001	Daniel J. Drucker	016777-0463	2882

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EXAMINER
PRIEBE, SCOTT DAVID

ART UNIT	PAPER NUMBER
1632	

DATE MAILED: 11/15/2002

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
09/833,740	Drucker et al.
Examiner	**Art Unit**
Scott D. Priebe, Ph.D.	1632

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Oct 23, 2002* .

2a) ☐ This action is **FINAL.** 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1-8* is/are pending in the application.

4a) Of the above, claim(s) *6-8* is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *1-5* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☒ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). *11*
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Election/Restriction

Claims 6-8 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to nonelected inventions, there being no allowable generic or linking claim. Election was made without traverse in Paper No. 13, filed 10/23/02.

Specification

The disclosure is objected to because of the following informalities:

Paragraph 0017 refers to Figure 1. However, there is no "Figure 1" *per se* in the drawings, but rather there are Figures 1a-1c. The description of Figure 3 in para. 0019 does not match the drawing labeled Figure 3. Rather the drawing Fig. 3 appears to correspond to the description of Figure 4 in para. 0020. The description of Fig. 4 in para. 0020 as a schematic does not match the drawing labeled Figure 4, which appears to show a Southern blot, as described in para. 0079. Para. 0024, as amended 10/18/01, incorrectly identifies the rat sequence as SEQ ID NO: 7 and the human sequence as SEQ ID NO: 8.

Para. 0078 refers to a shaded area in Fig. 2, however, Fig. 2 has no shaded areas. Para. 0098 refers to a solid black box in Fig. 7C, which has no shaded black box.

Appropriate correction is required.

The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01. See page 19, para. 0067; page 32, para. 0103.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-5 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. .

Claims 1-5 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1-5 are directed to a recombinant DNA construct comprising a promoter region of a GLP-2 receptor gene, (GLP-2R promoter). The specification (para. 0043) describes the

promoter as comprising at least 1000 bases upstream of the transcription start site, and including at least "the number of bases necessary to drive transcription at levels above detectable background", and desirably "transcription factor binding sites and upstream activator sequences, through which expression from the endogenous GLP-2R gene normally is regulated." The specification discloses a sequence of about 1.5 kb from upstream of the transcription start site (a SmaI-PstI fragment, nucleotides 182-1673 of SEQ ID NO: 1) of the mouse GLP-2R gene as being one embodiment. This is the only disclosed sequence that comprises at least 1000 bases upstream of the transcription start site of a GLP-2R gene. The specification discloses that the promoter of GLP-2R genes from other species, such as livestock and poultry, and mammals, especially human, are part of the invention, as are variants of these sequences, which may include truncations, extensions and deletions, but "which retain GLP-2R promoter function as determined by any of the assays herein described." The only assay disclosed in the specification relating to promoter function is to operably link the putative promoter sequence to a reporter gene, e.g. *lacZ*, make a transgenic mouse containing the construct and then compare the expression of the reporter to the expression of the endogenous mouse GLP-2R receptor in various tissues. However, the specification does not disclose what results of this assay would indicate that the putative promoter sequence is a "promoter of a GLP-2 receptor gene" required by the claimed invention. The specification at para. 0123 and 0124 discloses that the 1.5 kb mouse sequence directed expression of the reporter in similar but not identical tissues as the endogenous GLP-2R gene. Specifically, difference observed were that the endogenous gene, but

not the reporter, was expressed in pituitary; the reporter, but not the endogenous gene, was expressed in lung. Also, para. 0156 discloses that the number of cells in hippocampus and cerebellum expressing the endogenous gene and reporter gene were different. The specification discloses (para. 0156) that the 1.5 kb fragment may not have all of the DNA regulatory sequences required for correctly specifying "transgene transcription in all cells and tissues expressing the endogenous GLP-2R receptor."

Therefore, specification and claims do not clearly set forth the metes and bounds of "promoter region of a GLP-2 receptor gene" because it does not indicate what level of similarity in structure and in tissue expression between the putative promoter sequence and the endogenous promoter are required for the putative promoter to be considered a "promoter region of a GLP-2 receptor gene." It is unclear, especially from the teachings in para. 0156, whether the 1.5 kb mouse GLP-2R DNA fragment is a "promoter region of a GLP-2 receptor gene" since it did not "correctly specify transcription in all cells and tissues expressing the endogenous GLP-2R receptor." It is unclear how dissimilar a putative promoter sequence can be to an endogenous GLP-2R promoter in terms of both structure and function, and still be a "promoter region of a GLP-2 receptor gene" required by the claims. Consequently, the claims do not meet the requirements of §112, 2nd para.

The court and the Board have repeatedly held (*Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*,18 USPQ2d 1016 (CA FC, 1991); *Fiers v. Revel*, 25 USPQ2d 1601 (CA FC 1993); *Fiddes v. Baird*, 30 USPQ2d 1481 (BPAI 1993) and *Regents of the Univ. Calif. v. Eli Lilly & Co.*, 43

USPQ2d 1398 (CA FC, 1997)) that an adequate written description of a nucleic acid requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it, irrespective of the complexity or simplicity of the method; what is required is a description of the nucleic acid itself. It is not sufficient to define DNA solely by its principal biological property, because disclosure of no more than that, as in the instant case, is simply a wish to know the identity of any DNA with that biological property. Naming a type of material generically known to exist, in this case a "promoter region of a GLP-2 receptor gene," in the absence of knowledge as to what that material consists of, is not a description of that material. When one is unable to envision the detailed constitution of a complex chemical compound having a particular function, such as a nucleic acid, so as to distinguish it from other materials, as well as a method for obtaining it, conception has not been achieved until reduction to practice has occurred, i.e., until after the nucleic acid has been isolated. Thus, claiming all DNA's that achieve a result without defining what means will do so is not in compliance with the description requirement. Rather, it is an attempt to preempt the future before it has arrived.

The instant specification discloses at most a single species readable on a "promoter region of a GLP-2 receptor gene," the region upstream of the transcription start site in the mouse GLP-2R gene sequence shown in Fig. 1a-1b. However, as indicated above, it is unclear whether the 1.5 kb mouse GLP-2R DNA fragment from this region is a "promoter region of a GLP-2 receptor gene" required by the claims. If, as suggested in para. 0156, additional DNA regulatory sequences from the genome are required "to correctly specify transgene transcription in all cells

and tissues expressing the endogenous GLP-2R receptor," the specification does not describe these additional sequences. The specification discloses approximately 200 bases upstream of the transcription start site of the human GLP-2R gene, which was approximately 70% identical to the corresponding region of the mouse gene, and that the sequence upstream of this diverged. The upstream human sequence was not disclosed. However, as these two sequences are aligned in Fig. 7b, the sequence identity between the human and mouse sequences upstream of the transcription start site is only 54% (relative to the human sequence of 210 nucleotides). A best fit alignment performed by the Office of nucleotides 1-210 of SEQ ID NO: 7 (human) to nucleotides 1474-1665 of SEQ ID NO: 1 (mouse) yielded sequence identity of 67.5%. No structural information for the promoter of a GLP-2R gene for any other species of organism is disclosed. In the disclosed mouse (SEQ ID NO: 6) and human (SEQ ID NO: 7) sequences, several potential transcription factor recognition sequences are identified (Fig. 7b) for CdxA, GATA-1, NF-κB and Sp1, all of which occur within the first 180 nucleotides of the transcription start site. No information is presented as to whether these "putative" recognition sequences are in fact utilized in transcription, much less whether they are necessary or sufficient "to correctly specify transgene transcription." Also, no information is provided as to what other sequences upstream of the first 200 nucleotides are required "to specify correct transgene transcription" relative to an endogenous GLP-2R promoter. The specification does not identify those sequences in any GLP-2R promoter, including from mouse, that are necessary and sufficient to provide for correct function of a "promoter region of a GLP-2 receptor gene" Consequently, the specification

fails to identify any structural characteristics that would distinguish a "promoter region of a GLP-2 receptor gene" from other DNA sequences or promoters, i.e. those structural features of the recited promoter region that confer correct function.

While the specification provides characterization of the basal tissue expression profile of the endogenous mouse GLP-2R promoter (and the 1.5 kb fragment) in a mouse under normal laboratory conditions, it does not provide information on other factors that influence transcription, such as response to environmental conditions which alter the normal expression of the GLP-2R gene, e.g. response to inducers or suppressors of expression. Furthermore, it is unclear how the function of GLP-2R promoters from other organisms than mouse is to be assessed, in making a transgenic mouse or in making a transgenic organism of the organism from which the promoter was obtained, e.g. making a transgenic human to assess the function of a putative human GLP-2R promoter. The specification does not disclose assays using non-mouse transgenic organisms, nor does it provide tissue expression information on endogenous GLP-2R promoters in non-mouse organisms, e.g. human, chicken, toad, rattlesnake, earthworm, etc. The specification does not disclose which organisms even have a GLP-2R gene other than human, rats (and presumably most other mammals).

Therefore, the specification does not provide an adequate description of a generic a "promoter region of a GLP-2 receptor gene," either in terms of structure or function, and it is unclear whether it describes even a single species, mouse GLP-2R promoter, adequately, such that one of skill in the art would recognize that Applicant had possession of the invention as it is

broadly claimed, or that one could envision the recited GLP-2R promoter region from the description in the specification. The rejections under §112, 1st and 2nd paragraphs could be overcome by replacing "a promoter region of a GLP-2 receptor gene" with --a promoter comprising nucleotides 182-1673 of SEQ ID NO: 1--, which corresponds to the 1.5 kb fragment used in the examples.

Certain papers related to this application may be submitted to Art Unit 1632 by facsimile transmission. The FAX numbers are (703) 308-4242 or (703) 305-3014 for any type of communication. In addition, FAX numbers for a computer server system using RightFAX are also available for communications before final rejection, (703) 872-9306, and for communications after final rejection, (703) 872-9307, which will generate a return receipt. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 CFR 1.6(d)). NOTE: If applicant *does* submit a paper by FAX, the original copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED, so as to avoid the processing of duplicate papers in the Office.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Scott D. Priebe whose telephone number is (703) 308-7310. The examiner can normally be reached on Monday through Friday from 8 AM to 4 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Deborah Reynolds, can be reached on (703) 305-4051.

Any inquiry concerning administrative, procedural or formal matters relating to this application should be directed to Patent Analyst Patsy Zimmerman whose telephone number is (703) 308-8338. Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

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